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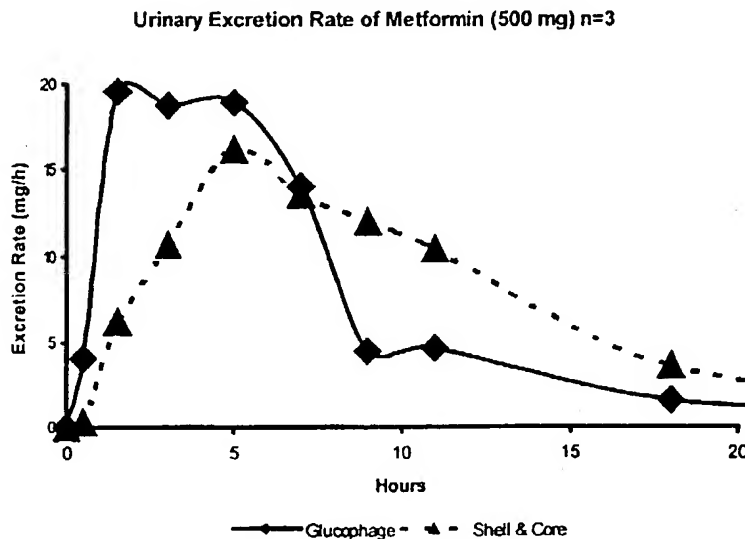
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- (71) Applicant: DEPOMED, INC. [US/US]; 366 Lakeside Drive, Foster City, CA 94404-1146 (US).
- (72) Inventors: BERNER, Bret; 239 El Granada Boulevard, El Granada, CA 94018 (US). LOUIE-HELM, Jenny; 30580 Mallorca Way, Union City, CA 94587 (US). GUSLER, Gloria; 20671 McClellan Road, Cupertino, CA 95014 (US). SHELL, John, N.; 3209 Outlook Drive, Rocklin, CA 95765 (US).
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(54) Title: SHELL-AND-CORE DOSAGE FORM APPROACHING ZERO-ORDER DRUG RELEASE



(57) Abstract: Drugs are formulated as oral dosage forms for controlled release in which the release rate limiting portion is a shell surrounding the drug-containing core. The shell releases drug from the core by permitting diffusion of the drug from the core. The shell also promotes gastric retention of the dosage form by swelling upon imbibition of gastric fluid to a size that is retained in the stomach during the postprandial or fed mode.

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*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

# INTERNATIONAL SEARCH REPORT

International Application No

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## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K9/20 A61K9/28

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, CHEM ABS Data, MEDLINE, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 55107 A (DEPOMED INC ;SHELL JOHN W (US); LOUIE HELM JENNY (US)) 10 December 1998 (1998-12-10) page 2, line 23 -page 3, line 19 page 3, line 32 - line 33; figure 5 page 4, line 30 -page 6, line 18; claims; examples 1,5	1-15, 22-30
X	DE 44 32 757 A (BOEHRINGER MANNHEIM GMBH) 21 March 1996 (1996-03-21) page 1, line 1 - line 20 page 1, line 50 - line 63 page 2, line 15 - line 67; claims; figure 1; examples 1-4,6-8	1-15, 22-30

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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

### \* Special categories of cited documents:

\*A\* document defining the general state of the art which is not considered to be of particular relevance

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\*P\* document published prior to the international filing date but later than the priority date claimed

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Date of the actual completion of the international search

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Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel: (+31-70) 340-2040, Tx: 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Marttin, E

# INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>WO 99 47128 A (SQUIBB BRISTOL MYERS CO)  23 September 1999 (1999-09-23)  page 1, line 14 - line 33  page 4, line 13 -page 5, line 11  page 9, line 20 -page 10, line 16  page 11, line 8 -page 12, line 10  page 13, line 17 - line 34  page 14, line 6 -page 16, line 15  page 16, line 34 -page 17, line 33  page 18, line 32 -page 20, line 15  page 28, line 16 - line 26  page 29, line 29 -page 30, last line;  claims; examples 1-3</p>	1-15, 22-30
X	<p>EP 0 526 862 A (VECTORPHARMA INT)  10 February 1993 (1993-02-10)</p> <p>page 4, line 13 - line 29  page 4, line 45 - line 53  page 5, line 1 - line 7  page 5, line 16 - line 36  page 5, line 41 - line 43  page 6, line 1 - line 53  page 7, line 20 - line 30  page 7, line 47 - line 53; claims  1,7,11-16,18-22; examples 2,5,6</p>	1-15,22, 23, 25-29, 31,33
X	<p>GB 1 428 426 A (PURDUE RESEARCH  FOUNDATION) 17 March 1976 (1976-03-17)</p> <p>page 1, line 5 - line 6  page 2, line 23 -page 5, line 18  page 6, line 58 -page 7, line 12  page 7, line 54 -page 8, line 8; claims  1,21,22,28-30,35,36; examples 1,3-5,7,9,10</p>	1-12, 22-29, 31,33
X	<p>US 5 151 273 A (KORSATKO-WABNEGG BRIGITTA  ET AL) 29 September 1992 (1992-09-29)</p> <p>column 2, line 13 - line 44; figure 3  column 2, line 55 -column 3, line 7  column 3, line 21 - line 36  column 3, line 61 -column 4, line 2;  claims; examples 4,5</p>	1,2, 6-13,22, 23,25-29
X	<p>WO 98 08515 A (JAGOTEC AG ;VERGNAULT GUY  (FR); DUFOUR ALAIN (FR); GRENIER PASCAL)  5 March 1998 (1998-03-05)  page 3, line 3 -page 5, line 34  page 7, line 26 -page 8, line 19; claims  1-3; example 1</p>	1,3-11, 13-15, 22,25-29

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

## Continuation of Box I.2

Present claims 1-12 and 22-34 relate to a composition defined by reference to two desirable characteristics or properties, namely first a solid polymeric matrix that swells upon imbibition of water to a size large enough to promote retention in the stomach while the stomach is in fed mode, and second when said dosage form is immersed in gastric fluid, said drug is released from said dosage form into said gastric fluid at a controlled rate limited at least in part by diffusion of said drug through said shell to an extent that at least about 40% of said drug remains unreleased one hour after such immersion has begun and substantially all of said drug is released within about twenty-four hours after such immersion has begun. Present claims 1-12 and 22-34 are lacking an essential feature and contain no technical feature allowing a search for these compositions. The two functional features, defining a result to be achieved, provide instructions that are insufficiently clear for the expert to reduce them to practice without undue burden. The results to be achieved cannot be directly and positively verified by tests specified in the description.

The claims cover all compositions having these characteristics or properties, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such compositions. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the compositions by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to the compositions prepared in examples 1-15 and those described in claims 13-21, and the concepts of: a solid polymeric matrix that swells upon imbibition of water to a size large enough to promote retention in the stomach while the stomach is in fed mode; and when said dosage form is immersed in gastric fluid, said drug is released from said dosage form into said gastric fluid at a controlled rate limited at least in part by diffusion of said drug through said shell to an extent that at least about 40% of said drug remains unreleased one hour after such immersion has begun and substantially all of said drug is released within about twenty-four hours after such immersion has begun.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

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